

REMARKS

In the Office Action, the Examiner again rejected all pending claims 1-9. Specifically, the Examiner cited combinations of the Karageozian, Knepper, and Yasuyuki references with other formerly cited references as rendering the present invention obvious under 35 USC 103(a). Applicant respectfully traverses these rejections in view of the following remarks.

Three criteria must be met in order to establish a case of prima facie obviousness:

1) the references must teach or suggest all the claim limitations, 2) there must be some suggestion or motivation to modify or combine references, and 3) there must be a reasonable expectation of success. A reasonable reading of the references cited by the Examiner indicates that taken together, the references do not satisfy the above-criteria.

The Examiner rejects claims 1, 2, 3 and 7-9 under 35 USC 103(a) as being unpatentable over Karageozian in view of Knepper et al. and Yasuyuki et al.

Karageozian discloses using hyaluronidase derived from the bovine testicle to accelerate the clearance of hemorrhagic blood. Knepper discloses infusing rabbits' eyes with Streptomyces hyaluronidase in order to decrease aqueous outflow resistance, and Yasuyuki discloses the production of hyaluronidase from Streptomyces Hyalurolyticus.

The Examiner asserts that it would have been obvious to one of ordinary skill in the art to use a purified form of hyaluronidase derived from Streptomyces hyalurolyticus as taught by Yasuyuki et al. to modify Karageozian's method of clearing hemorrhagic blood by using hyaluronidase derived from Streptomyces instead of bovine testes because Knepper discloses that Streptomyces hyaluronidase is more effective than testicular hyaluronidase

in decreasing outflow resistance in the eye. Applicant respectfully disagrees with this assertion.

Karageozian in view of Knepper and Yasuyuki do not teach or suggest the limitations of the claimed invention. The Examiner acknowledges that Karageozian fails to disclose a method utilizing a hyaluronidase derived from Streptomyces to treat optical disorders. In fact, Karageozian actually teaches away from the present invention in that it discloses using hyaluronidase derived from bovine testicles, which is exactly what the present invention is trying to avoid. Knepper fails to disclose using hyaluronidase from Streptomyces to clear hemorrhagic blood from the eye and/or to stimulate flow of physiological fluids from the eye. Knepper only suggests that Streptomyces hyaluronidase is more effective than testicular hyaluronidase at reducing aqueous outflow resistance. Yasuyuki merely discloses a method of producing purified hyaluronidase, and neither teaches nor suggests using hyaluronidase to treat eye disorders.

Karageozian in view of Knepper and Yasuyuki do not provide motivation to combine the references. Karageozian is complete in teaching clearing of hemorrhagic blood from the eye using testicular hyaluronidase and actually teaches away from the present invention because testicular hyaluronidase is the exact substance that the present invention does not want to use. The Examiner assumes that since testicular hyaluronidase has been used in the art to treat eye disorders, it is obvious that streptomyces hyaluronidase would do the same; however Applicant disagrees with this assumption. The law states that a presumption of obviousness based on a reference disclosing structurally similar compounds may be overcome where there is evidence showing there is no reasonable expectation of similar properties in structurally similar

compounds. *In re May*, 574 F.2d 1082, 197 USPQ 601 (CCPA 1978). As pointed out in Yasuyuki, columns 5 and 6 and Table 2, Streptomyces hyaluronidase and testicular hyaluronidase are similar compounds of different derivations that are known to have different characteristics such as different heat stability, different optimal pH, and different inhibitors. As explicitly stated in Yasuyuki, column 6, lines 30-33, the hyaluronidase produced by Streptomyces hyalurolyticus is proved to be clearly different from that of bacteria and animal. Further, Streptomyces hyaluronidase was originally believed to be medically inapplicable due to protease inactivation—a key contrast to testicular hyaluronidase. Applicant asserts that these facts are sufficient evidence that it is not reasonable to assume that Streptomyces hyaluronidase can be used to treat all the disorders treatable by testicular hyaluronidase disclosed by Karageozian or any other reference cited by the Examiner. Knepper at most suggests that Streptomyces hyaluronidase can be used in the eye but suggests no uses for Streptomyces hyaluronidase beyond reducing aqueous outflow resistance, while Yasuyuki suggests nothing regarding using Streptomyces hyaluronidase to treat eye disorders. In fact, as stated above, Yasuyuki points out the distinct differences between the two hyaluronidases, and, if anything, suggests that the hyaluronidases would not be used to treat the same disorders.

Lastly, there is no reasonable expectation of success of using Streptomyces hyaluronidase with the method of Karagozian to clear hemorrhagic blood or stimulate physiological fluid flow of the eye since the Streptomyces hyaluronidase and testicular hyaluronidase have different characteristics and since it was widely believed in the art that Streptomyces hyaluronidase had no medical applicability. The present invention

unexpectedly found that purified Streptomyces hyaluronidase had enzyme activity levels so high and protease activity levels so low so as to allow medical applications of Streptomyces hyaluronidase in a low-protease environment such as the eye. Specifically, the present invention discloses that such purified Streptomyces hyaluronidase could be used to clear hemorrhagic blood, stimulate eye fluid flow, soften the cornea, spread local anesthesia throughout the ocular tissue, and isolating collagen to produce contact lenses. The results were unexpected, therefore there was no reasonable expectation of success. Claim 2 has been cancelled in order to direct the claims to specific eye disorders.

Given the above facts, Applicant asserts that claims 1, 2, 3 and 7-9 are not obvious in view of Karageozian, Knepper, and Yasuyuki. Further, while the Examiner rejected claim 4 as unpatentable over Karageozian in view of Knepper, Yasuyuki, and Harris et al., rejected claim 5 as unpatentable over Karageozian in view of Knepper, Yasuyuki, and Straus, and rejected claim 6 as unpatentable over Karageozian in view of Knepper, Yasuyuki, and Federov, Applicant asserts that Harris et al., Straus, and Federov do not overcome the shortcomings of Karageozian, Knepper, and Yasuyuki discussed above. Specifically, Applicant asserts that based on the law and facts discussed above, sufficient evidence has been provided that it is not reasonable to presume that disorders treated by testicular or bacterial hyaluronidase will be treated by Streptomyces hyaluronidase.

In sum, Streptomyces hyaluronidase was previously thought to be medically inapplicable, the present invention unexpectedly found that purified Streptomyces hyaluronidase could be medically applicable in low-protease environments, Streptomyces hyaluronidase and testicular hyaluronidase are known to have different characteristics;

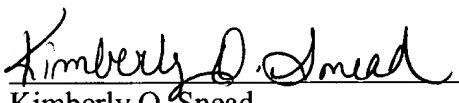
therefore, the references set forth against the present invention do not render obvious the use of Streptomyces hyaluronidase to treat specific eye disorders because the references do not, alone or in combination, teach or suggest all limitations of the present invention.

CONCLUSION

In light of the above amendments and arguments, Applicant respectfully asserts that the present application is now in condition for allowance. Accordingly, Applicant requests that all rejections be withdrawn and a Notice of Allowance be issued.

Respectfully submitted,

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